

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference K 3176	FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/EP2004/003538	International filing date (day/month/year) 02.04.2004	Priority date (day/month/year) 03.04.2003	
International Patent Classification (IPC) or national classification and IPC C07K14/435, C12N15/12, C12N15/63, C12N15/74, C12N15/79, A01K67/027, A61K38/17, A61K48/00, C12Q1/68, G01N33/53			
Applicant DEUTSCHES KREBSFORSCHUNGSZENTRUM STIFTUNG DES ...			
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 8 sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (Indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).			
4. This report contains indications relating to the following items: <div style="margin-left: 20px;"> <input checked="" type="checkbox"/> Box No. I Basis of the opinion <input type="checkbox"/> Box No. II Priority <input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input checked="" type="checkbox"/> Box No. VII Certain defects in the international application <input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application </div>			
Date of submission of the demand 11.08.2004	Date of completion of this report 01.03.2005		
Name and mailing address of the International preliminary examining authority: <div style="margin-left: 20px;">  European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840 </div>	Authorized Officer Mateo Rosell, A.M. Telephone No. +49 30 25901-319		



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/003538

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-52 as originally filed

Sequence listings part of the description, Pages

1-30 received on 26.09.2003 with letter of 26.09.2003

Claims, Numbers

1-20 as originally filed

Drawings, Sheets

1-27 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify):*
 - ☐ any table(s) related to sequence listing *(specify):*
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify):*
 - ☐ any table(s) related to sequence listing *(specify):*

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-14,16-20
	No: Claims	15
Inventive step (IS)	Yes: Claims	1-14,16-20
	No: Claims	15
Industrial applicability (IA)	Yes: Claims	1-20
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY REPORT
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Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☒ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☒ received by this Authority as an amendment on
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: DATABASE EMBL [Online] 4 September 2002 (2002-09-04) Database accession no. AF535142

D2: DATABASE EMBL [Online] 29 October 2002 (2002-10-29) Database accession no. AF495910

-& ZHANG ET AL.,: 'The nesprins are giant actin-binding proteins, orthologous to Drosophila melanogaster muscle protein MSP-300.' GENOMICS, vol. 80, no. 5, 2002, pages 473-481,

-& ZHANG ET AL., : 'Nesprins a novel family of spectrin-repeat-containing proteins that localize to the nuclear membrane in multiple tissues.' JOURNAL OF CELL SCIENCE, vol. 114, no. 24, 2001, pages 4485-4498.

D3: DATABASE EMBL [Online] 7 February 2001 (2001-02-07) Database accession no. AB051543

D4: DATABASE EMBL [Online] 20 March 2002 (2002-03-20) Database accession no. AL713682;

D5: DATABASE EMBL [Online] 28 June 2002 (2002-06-28) Database accession no. AX430417 & WO 02 40715 A (INCYTE GENOMICS INC.) 23 May 2002

D6: DATABASE EMBL [Online] 28 June 2002 (2002-06-28) Database accession no. AX430670 & WO 02 40715 A (INCYTE GENOMICS INC.) 23 May 2002

D7: DATABASE EMBL [Online] 26 July 2001 (2001-07-26) Database accession no. AAI59698 & WO 0 153312 A (HYSEQ INC.) 26 July 2001

D8: DATABASE EMBL [Online] 22 October 2001 (2001-10-22) Database accession no. AAI57912 & WO 0 153312 A (HYSEQ INC.) 26 July 2001

D9: DATABASE EMBL [Online] 22 October 2001 (2001-10-22) Database accession no. AAM40542 & WO 0 153312 A (HYSEQ INC.) 26 July 2001

D10: DATABASE EMBL [Online] 22 October 2001 (2001-10-22) Database accession no. AAM38756 & WO 0 153312 A (HYSEQ INC.) 26 July 2001

D11: DATABASE EMBL [Online] 15 February 2002 (2002-02-15) Database accession no. AAS90431 & WO 0 175067 A (HYSEQ. INC) 11 October 2001

- D12: DATABASE EMBL [Online] 13 February 2002 (2002-02-13) Database accession no. AAS90799 & WO 0 175067 A (HYSEQ INC) 11 October 2001
- D13: DATABASE EMBL [Online] 18 February 2002 (2002-02-18) Database accession no. ABG26244 & WO 0 175067 A (HYSEQ INC.) 11 October 2001
- D14: EP-A-1 293 569 (RES ASS FOR BIOTECHNOLOGY ;HELIX RES INST (JP)) 19 March 2003
- D15: DATABASE EMBL [Online] 14 July 2003 (2003-07-14) Database accession no. AX780848 & WO 03 039443 A (DEUTSCHES KREBSFORSCHUNGS-ZENTRUM) 15 May 2003

Novelty (Art 33(2) PCT)

In view of D1-D15 :

D1 (Homo sapiens enaptin mRNA: 99.9% identity in 10001 bp and 99.44% identity in 3048 aa overlap with SEQ.ID.N.9 and 30, respectively), **D2** (H. sapiens nesprin-1 mRNA: 99.9% identity in 9422 bp and 99.21% identity in 3055 aa overlap with SEQ.ID.N.9 and 30, respectively), **D3** (KIAA1756 protein: 100% identity in 2985 bp overlap with SEQ.ID.N.9), **D4** (clone DKFZp547N107: 99.75% in 2891 bp overlap with SEQ.ID.N.9), **D5** (SEQ.ID.N. 199 from WO0240715: 100% identity in 1993 bp overlap with SEQ.ID.N.9), **D6** (SEQ.ID.N. 425 from WO0240715: 96.38% identity in 664 aa overlap with SEQ.ID.N.30), **D7** (SEQ.ID.N. 3687 from WO00153312: 99.95% identity in 2098 bp overlap with SEQ.ID.N.9), **D8** (SEQ.ID.N. 115 from WO00153312: 99.95% identity in 2098 bp overlap with SEQ.ID.N.9), **D9** (SEQ.ID.N. 5473 from WO00153312: 99.71% identity in 699 aa with SEQ.ID.N.30), **D10** (SEQ.ID.N. 1901 from WO00153312: 99.57% identity in 698 aa overlap with SEQ.ID.N.30), **D11** (SEQ.ID.N. 26235 from WO00175067: 99.66% identity in 2098 bp overlap with SEQ.ID.N.9), **D12** (SEQ.ID.N. 26603 from WO00175067: 94.08% identity in 4143 bp overlap with SEQ.ID.N.9), **D13** (SEQ.ID.N. 56603 from WO00175067: 99.14% identity in 699 aa overlap with SEQ.ID.N.30), **D14** (SEQ.ID.N. 399 and 2038 from EP1293569: 99.9% identity in 1653 bp overlap and 98.87% identity in 534 aa overlap with SEQ.ID.N.9 and 30, respectively) and **D15** (SEQ.ID.N. 3005 from WO03039443: 99.36% identity in 2985 bp overlap with SEQ.ID.N.9):

the present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 15 is not new in the sense of Article 33(2) PCT.

To overcome the novelty objection to claim 15 A) a) and 15 A) b), this claim should be redrafted by replacing the term 'comprises' by 'consists of' and 'comprising' by 'consisting of'.

Inventive step (Art. 33(3) PCT)

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 15A) e) does not involve an inventive step in the sense of Article 33(3) PCT.

Fragments *per se* are not inventive. The fragments limited to their 'biological activity' as defined below might allow the acknowledgment of an inventive step.

Re Item VII

Certain defects in the international application

Lack of disclosure (Art. 5 PCT)

1. Claim 16 refers to compounds (activator/agonist) obtained by screening methods, i.e. it refers to compounds without giving a true technical characterization. Moreover, no such compounds are defined in the application. In consequence, the subject-matter of said claim is **not** sufficiently disclosed and supported.
2. Claims 18 and 19 do not comply with Art 5 PCT for the following reasons; Since the only biological property which has been shown in the examples is a **lower expression of Drop1 in ovarian, mammary, stomach, lung, kidney and thyroidea carcinomas** (see example 4 and example 5, 2nd paragraph), the scope of claim 18

should be limited to epithelial tumors and that of claim 19 should be limited to the above mentioned carcinomas, whilst cervical, pancreas and testis carcinomas should be deleted from these claims.

Re Item VIII

Certain observations on the international application

Clarity (Art. 6 PCT)

1. Claims 1,15 relate to the amino acid and nucleic acid sequences of the human dystrophin-related protein from present application (Drop1) as depicted in Figure 10 and Figure 6B, respectively. The amino acid sequence could be unambiguously identified as SEQ.ID.N.30, whereas the nucleic acid sequence could not. In fact, the description refers to 'an open reading frame of 9.099 bp' (see example 9) while the on 26.09.2003/10.08.2004 submitted sequence listing contains a nucleic acid sequence of 10001 bp in length (SEQ.ID.N.9) which the ISA assumes should correspond to the nucleotide sequence of the human Drop1 protein. This inconsistency, together with some inconsistencies found in Figure 6B between the given nucleic acid lengths of Drop1alpha pGFP#4 (1213 bp), Drop1beta#3 (2472 bp), Drop1gamma#4 (2561 bp), Drop1epsilon#1 (1514) and the submitted sequence listing, leads to a lack of clarity within the meaning of Article 6 PCT.

It has been assumed that the nucleotide sequence of Drop1 corresponds to SEQ.ID.N.9.

2. Claim 6 and 7 should refer to polypeptide and polynucleotide, respectively, of claim 1. Drop1 has no true technical meaning if devoided of its SEQ. ID.